REMARKS/ARGUMENTS

Claims 11-23, 25 and 27-33 are pending. For convenience, the Examiner's rejections are addressed in the order presented in the March 18, 2003 Office Action.

I. Status of the claims

Claims 11-23 are cancelled without prejudice to subsequent revival.

II. Rejections under 35 U.S.C. §101

Claims 25 and 27-33 are rejected under 35 U.S.C. §101 because, allegedly, the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. According to the Office Action, although the application teaches that the claimed Mkinase is involved in the cell cycle, there is no teaching of the effects of Mkinase on the cell cycle. Similarly, the Office Action asserts that the claimed nucleic acids lack a well established utility.

Applicants respectfully traverse the rejection. The Office Action has not put forth a *prima facie* case in support the assertion of lack of utility of the claimed invention. In addition, Applicants submit evidence to support the utility originally asserted in the application as filed.

A. Standard to Assess Utility

According to MPEP §2107, the Examiner should review the claims and the supporting written description to determine whether the utility requirement under 35 U.S.C. §101 is met. No rejection based on lack of utility should be made if an invention has a well-established utility, *i.e.*, a utility that will be immediately appreciated by one of ordinary skill in the art based on the characteristics of the invention, regardless any such utility has been asserted. Neither should any rejection be made for lack of utility if an applicant has asserted a specific and substantial utility that would be considered credible by one of ordinary skill in the art.

In most cases, an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101. MPEP §2107.02 III A. The Court of Customs and Patent Appeals stated in *In re Langer*:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of §101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

In re Langer, 183 USPQ 288, at 297 (CCPA, 1974, emphasis in original). To overcome the presumption of sufficient utility as asserted by an applicant, the Examiner must carry the initial burden to make a *prima facie* showing of lack of utility and provide a sufficient evidentiary basis for the conclusion. In other words, the Examiner "must do more than merely question operability--[he] must set forth factual reasons which would lead one skilled in the art to question objective truth of the statement of operability." *In re Gaubert*, 187 USPQ 664, 666 (CCPA 1975).

MPEP §2107.02 IV further states, a detailed explanation should be given for a utility rejection as to why the claimed invention has no specific and substantial asserted utility. Documentary evidence should be provided when possible. Otherwise the Examiner should specifically explain the scientific basis for his factual conclusions.

B. The Asserted Utility Is Specific and Substantial

The present specification provides, for the first time, the cloning of a nucleic acid that encodes an Mkinase polypeptide. Pending claims are drawn to nucleic acids encoding Mkinase polypeptides, *i.e.*, cell cycle proteins. It is specifically asserted that the Mkinase cell cycle proteins encoded by the claimed nucleic acids are useful to diagnose, treat or prevent cell cycle associated disorders, including cancer. (*See, e.g.*, page 40 lines 12-17 of specification). The specification also states that the availability of nucleic acid sequences that encode Mkinase cell cycle proteins enables assay systems to identify compounds that modulate Mkinase activity, thereby modulating the cell cycle. (*See, e.g.*, page 31 lines 2-29 of the specification).

Applicants assert that the present invention has a specific utility. Specific utility is defined by the MPEP as a utility that is specific to the subject matter claimed. The MPEP explains that applications show sufficient specific utility when applicants disclose a "specific biological activity" and reasonably correlate that activity to a "disease condition." MPEP

§§2107.01 and 2107.02. In the present application, Applicants disclose a "disease condition," *i.e.*, a proliferative disorder, in particular cancer, that correlates with a "biological activity," including kinase activity, ability to affect the cell cycle, modulation of pathways involved in tumor progression, and TRAF protein binding. (*See e.g.*, specification at page 31, lines 3-7.) This application demonstrates that Mkinase cell cycle proteins have kinase activity and bind to TRAF4, a protein with a demonstrated role in the cell cycle and tumor progression. (*See, e.g.*, specification at page 2, lines 17-18 and page 53, lines 14-16) The application further provides methods for identifying compounds capable of modulating Mkinase cell cycle protein activities, which may be used for treating proliferative diseases, including cancer, and methods to diagnose such diseases by detecting changes in the chromosomal Mkinase gene. (*See, e.g.*, specification at page 31, line 12 through page 32, line 14, and page 21, lines 4-9.) Applicants thus submit that the present invention has a specific utility, *e.g.*, Mkinase cell cycle proteins can effect the cell cycle and therefore are targets for development of, for example cancer therapeutics. In addition, polymorphisms in the chromosomal Mkinase gene are associated with cancer and can be used to diagnose that disease. These activities are clearly specific for the claimed nucleic acids and not any nucleic acid that encodes a kinase.

Applicants also assert that the present invention has a substantial utility or a "real-world" use. The present invention provides Mkinase cell cycle proteins, demonstrates that Mkinase cell cycle proteins have cell cycle activity, and teaches how to identify modulators of Mkinase cell cycle proteins. Therefore, there is a real-world use of the invention in the modulation of the cell cycle, as well as in the identification of compounds that modulate Mkinase cell cycle proteins and thus are useful as therapeutic agents for treating diseases related to altered cell proliferation, such as cancer.

C. The Examiner Has Not Established A *Prima Facie* Showing of Lack of Utility

The Examiner's rejection of the pending claims for alleged lack of utility was based on the repeated statement that no evidence in the specification or prior art demonstrates a role for Mkinase cell cycle proteins in the cell cycle or an affect of Mkinase on cell proliferation.

Simply put, the Examiner did not believe the specific and substantial utility asserted by Applicants.

Applicants respectfully submit that raising a rejection for lack of utility in such a manner is inconsistent with the proper practice described in the MPEP, which places the initial burden on the Examiner, not Applicants, to provide evidence to support a factual conclusion of the credibility of an asserted utility. In fact, MPEP §2107.02 III.B. specifically cautions Office personnel that, once an assertion of a particular utility is made, "that assertion cannot simply be dismissed ..... as 'wrong,' even when there may be reason to believe the assertion is not entirely accurate." Instead, the Examiner must provide an explanation setting forth the reasoning used in concluding that the asserted specific and substantial utility is not credible; support for factual findings relied upon in reaching the conclusion; and an evaluation of all relevant evidence of record, including utilities taught in the closest prior art. MPEP §2107.02 IV.

The Examiner provided none of the above. Applicants respectfully submit that a *prima facie* showing of lack of utility is not established and the rejection thus cannot properly stand.

D. The previously asserted Mkinase cell cycle protein utility of cell cycle regulation and association with cancer is correct.

In support of the utility asserted in the application as filed, Applicants submit as Exhibit A the following published journal article: Kato *et al.* Genomics 79:760-767 (2002). Kato *et al.* disclose a human N-terminal kinase like (NTKL) nucleic acid and encoded protein. Starting with the first encoded methionine of the claimed sequences, the nucleic acid and amino acid sequences of Kato *et al.* share 99% identity with the claimed nucleic acid and amino acid sequences. Thus, the claimed nucleic acids and encoded proteins are the same as the NTKL nucleic acids and encoded proteins.

Kato *et al.* demonstrate that the NTKL gene maps to a chromosome 11 region known to contain breakpoint for chromosome translocations reported in extragonadal germ cell tumors and renal cell carcinomas. (See. *e.g.*, Kato *et al.* at page 762.) Thus, NTKL gene, *i.e.*, the Mkinase gene, is associated with cancer. Kato *et al.* also demonstrate that a related isoform

of the NTKL protein localizes to the centrosomes during mitosis, strongly suggesting that NTKL proteins *i.e.*, Mkinase cell cycle proteins, have a role in the cell cycle.

Kato *et al.* reported that the NTKL protein did not have kinase activity. Applicants reassert that Mkinase cell cycle proteins have kinase activity that is detectable under specific experimental conditions. (See, *e.g.*, specification at page 53 lines 14-16 and declaration of Dr. Xiang Xu, submitted October 21, 2001.) Applicants also assert that the presence or absence of kinase activity in Mkinase cell cycle proteins, does not affect the utility of the Mkinase nucleic acids to detect polymorphisms in the genomic Mkinase nucleic acid, thereby diagnosing cancer.

The Office Action also appears to assert that in order to establish utility, Mkinase must be defined as a positive or a negative regulator of the cell cycle. (Office Action at pages 3-4.) Applicants respectfully submit that an assertion of cell cycle regulatory function is sufficient to meet the utility requirement under 35 U.S.C. §101, and that modulators, *e.g.*, inhibitors, of a cell cycle regulator, such as Mkinase, also have utility. For example, an inhibitor of a positive cell cycle regulator is useful for treatment of diseases such as cancer. Similarly, an inhibitor of a negative regulator of the cell cycle is useful for treatment of hypoproliferative diseases or to promote wound healing. Thus, the asserted utilities for both Mkinase and modulators of Mkinase meet the utility requirement under 35 U.S.C. §101.

In view of the above arguments and evidence, Applicants respectfully request that the Mkinase utility disclosed in the application as filed is correct and request that the rejection under 35 U.S.C. §101 be withdrawn.

III. Rejections under 35 U.S.C. §112, first paragraph, enablement

Claims 25 and 27-33 are rejected under 35 U.S.C. §112, first paragraph as allegedly lacking enablement. Specifically, the Office Action alleges that the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility, and that one of skill would not know how the use the claimed invention.

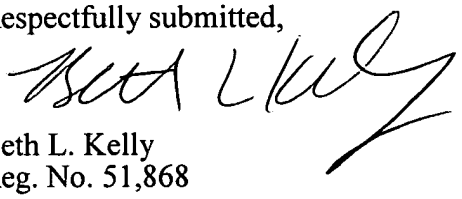
Applicants have submitted arguments and evidence in support of the Mkinase utility asserted in the application as filed in Section II of this response. In view of those arguments and evidence, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph also be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at 415-576-0200.

Respectfully submitted,



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